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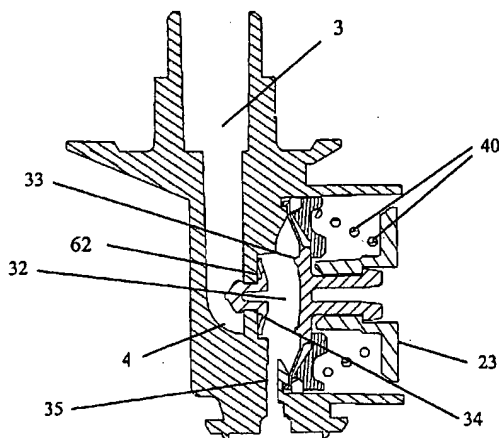
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(54) Title: DIAPHRAM METERING CHAMBER DISPENSING SYSTEMS



(57) Abstract: This invention describes a method and apparatus for a dispenser assembly (1) suitable for dispensing reagent in an automatic system. In embodiments, the present invention may include a metering chamber (32) that accurately controls the amount of fluid dispensed. In other embodiments, the amount of fluid may be controlled by the action of a flexible diaphragm (33), which may be assembled into a cavity of a dispenser housing creating a metering chamber. In another embodiment, a volume created by a metering chamber may determine the volume of dispensed fluid. When a diaphragm is compressed from its free or uncompressed position (36) to an inverted or compressed position (37), it may substantially conform to the inner surface of the metering chamber. Fluid enters a metering chamber through an inlet unidirectional valve (34) and exits a metering chamber through an outlet unidirectional valve (25).



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DIAPHRAGM METERING CHAMBER DISPENSING SYSTEMS

This is a PCT application claiming the benefit of United States of America Provisional Application No. 60/477,382, filed 09 June 2003, hereby incorporated by
5 reference.

I. TECHNICAL FIELD

This invention relates to liquid dispensing systems and other devices which may
10 be interchangeable and for dispensing small amounts of a liquid, such as a biological reagent, chemical reagent, or the like. The invention may include a liquid dispensing cartridge pump and methods for dispensing small amounts of liquids. It may also be applied specifically to automated systems for the pathology laboratory to perform special stains, immunohistochemical stains (IHC), or In Situ Hybridization (ISH).
15

II. BACKGROUND OF THE INVENTION

It is understood that there are general methods for dispensing reagents in an automated system, including but not limited to, a repetitive non-disposable dispensing
20 assembly design and a disposable dispensing assembly design. In one aspect, a repetitive non-disposable design may use pumps and tubing. One example may include an automated pipette. A pipetting device may draw fluid from a bottle and release the fluid onto the sample. This type of design may be cost effective since the reagents may be packaged in the same bottles and long-term material compatibility issues may be
25 minimized. Among the disadvantages of non-disposable designs may be the continued maintenance to clean and flush tubing to prevent carryover and cross contamination. Further, a disadvantage may include exposure of reagents to air which can reduce their useful shelf-life.

30 A disposable design, generally, may be understood to include a syringe pump assembly. This design may also be known as a "piston plunger". Some disadvantages of this design may be that a force required to depress a plunger can vary significantly and piston plunger dispensers can be susceptible to leakage due to tolerance and material

compatibility issues. A plunger may employ an elastomeric seal, which may contact a syringe barrel, possibly providing a sliding or dynamic seal to retain fluid. From one perspective, this design may be applicable only for a limited number of reagents and chemicals that are compatible with the elastomeric seal, but it may not be adequately
5 useful for a broad range of chemicals that may cause the seal to shrink or swell. However, tolerances required for proper operation of this kind of seal can be difficult to achieve in standard manufacturing processes and it is at this interface that material compatibility concerns may have adverse effects possibly leading to leakage if the elastomer shrinks or binding if the elastomer swells.

10

U.S. Pat. No. 4,844,868 to Rokugawa, U.S. Pat. No. 5,232,664 to Krawzak et al., and U.S. Pat. No. 6,045,759 to Ford et al., appear to have somewhat attempted to modify a form of a syringe pump. Each of these devices can draw fluid into a syringe through a check valve and may be dispensed through a second check valve. From one perspective,
15 each of the disadvantages noted above for syringe pumps apply here as they may relate to tolerance and material compatibility concerns. In addition, a design noted in U.S. Pat. No. 6,045,759 to Ford et al. appears to have the disadvantage that a vacuum created in the reagent reservoir should be released since a chamber may not be adequately collapsible. Some methods for vacuum release may be prone to blockage, tolerance
20 issues, and may allow air to come in contact with the reagents. If air is in contact with a reagent, it may cause a decrease in the performance and stability of the reagent.

U.S. Pat. Nos. 5,645,114 and 5,316,452, both to Bogen et al. and U.S. Pat. Nos. 6,092,695 and 6,244,474 to Loeffler may include a liquid dispensing pump and a
25 metering chamber attached to a liquid reservoir. While some systems may have a syringe pump design, other systems appear to have a compressible elastomeric metering chamber connected to a liquid reservoir and may include a flexible bag supported within a rigid housing. From one perspective these systems may have the following disadvantages: the materials utilized for flexible bags may not be adequately robust and
30 can be susceptible to punctures, sealing failures, and material compatibility issues; the materials utilized for flexible bags can be susceptible to breakage due to the rigors of shipping; the compressible metering chamber, made of an elastomer, may have the disadvantages of permeability, dimensional inaccuracy, and failures related to material

incompatibility; the capacity of the metering chamber can be much larger than the desired dispense volume; and the volume of the fluid dispensed may be determined by the dispensing mechanism on the automated system. Further, accuracy of the dispenser can be significantly impacted by the calibration of a dispensing mechanism on an automated system.

Previous devices do not adequately address issues related to reagent stability, material incompatibility, vacuum created when drawing fluid from a liquid reservoir, shipping robustness, and dispense accuracy, among others as addressed in the present invention.

III. DISCLOSURE OF THE INVENTION

The present invention relates to a liquid dispensing system and other devices which allow for the dispensing of small amounts of liquids in an automated system. Systems may include a reservoir connected to a compressible metering chamber. A flexible diaphragm may compress or extend and uncompress or move to a free state while measuring and dispensing a precise amount of fluid.

It is an object of the present invention to provide a dispensing system that allows for vacuum build up while keeping an air-tight enclosed environment.

It is another object of the present invention to provide an accurate and repeatable dispensing system.

It is yet another object of the invention to provide a dispensing system that optimizes energy efficiency and utilizes less moving parts with a reduced amount of friction.

It is an object of the invention to provide an interchangeable liquid dispensing cartridge pump.

It is yet another object of the invention to provide an automated dispensing system.

Naturally, further goals and objects of the invention are disclosed throughout
5 other areas of the specification and claims.

IV. BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other objects, features and advantages of the invention will be
10 apparent from the following more particular description of the invention, as illustrated in the accompanying drawings.

Figure 1 shows a sectional view of an embodiment of the invention of a reservoir
and dispenser assembly.
15

Figure 2 shows a side view of an embodiment of the invention of a reservoir
without housing and a dispenser assembly.

Figure 3 shows an embodiment of the invention of a reservoir and housing
20 assembly.

Figure 4 shows a partial view of an embodiment of the invention of a dispenser
assembly.

Figure 5 shows a sectional, partial view of an embodiment of a dispenser
25 assembly without a reservoir and outlet unidirectional valve.

Figure 6 shows a sectional view of an embodiment of an outlet unidirectional
valve assembly.
30

Figure 7 shows a sectional view of an embodiment of a diaphragm in a free state
or uncompressed state.

Figure 8 shows a sectional view of an embodiment of a diaphragm in a compressed state.

Figure 9 shows a sectional view of an embodiment of a metering chamber having
5 an open inlet unidirectional valve and a closed outlet unidirectional valve.

Figure 10 shows a sectional view of an embodiment of a metering chamber having a closed inlet unidirectional valve and an open outlet unidirectional valve.

10 Figure 11 shows a perspective view of an embodiment of a reservoir housing connected to a dispenser assembly and an unassembled dual clamp element.

Figure 12 shows a perspective view of an embodiment of an assembled reservoir housing.
15

Figure 13 is side view of a collapsible molded reservoir in an expanded state.

Figure 14 is a side view of a collapsible molded reservoir in a partially collapsed state.
20

V. MODE(S) FOR CARRYING OUT THE INVENTION

As mentioned earlier, the present invention includes a variety of aspects, which may be combined in different ways. The following descriptions are provided to list
25 elements and describe some of the embodiments of the present invention. These elements are listed with initial embodiments, however it should be understood that they may be combined in any manner and in any number to create additional embodiments. The variously described examples and preferred embodiments should not be construed to limit the present invention to only the explicitly described systems, techniques, and
30 applications. Further, this description should further be understood to support and encompass descriptions and claims of all the various embodiments, systems, techniques, methods, devices, and applications with any number of the disclosed elements, with each

element alone, and also with any and all various permutations and combinations of all elements in this or any subsequent application.

5 In embodiments, a liquid dispenser apparatus and methods of dispensing liquids may include a liquid reservoir (11) and may even provide for establishing liquid in a reservoir. A reservoir may be a receptacle, chamber or the like containers for holding a liquid or fluid. A reservoir may be located near a dispenser assembly (1) or may even be remote and may be fluidly connected to a compressible metering chamber (32). A compressible metering chamber may move from between a compressed and
10 uncompressed position and may even include a compressible diaphragm. In other embodiments, a reservoir may be located above a metering chamber. A metering chamber may be a compartment, cavity or closed space that may be used for measuring an amount of liquid or fluid. In embodiments, a metering chamber (32) may be connected to a reservoir with a liquid introduction element (3) such as seen in Fig. 1. A
15 liquid introduction element may include tubing, a channel (6) or the like fluid flowing element. Fluid may enter a metering chamber through an upper or inlet unidirectional valve (34) or similar type element and may exit a metering chamber through a lower or outlet unidirectional valve (25) or similar type element.

20 It may be desirable to provide a sealed system from a reservoir to an outlet unidirectional valve. Outside air may cause chemical degradation and may damage or impair tests or samples that may be used in conjunction with a dispenser system. As such, the present invention, in embodiments, may provide for sealingly attaching a metering chamber to a reservoir and may provide a seal (5) located between a reservoir
25 and a liquid introduction element (3). A connection or connections between a reservoir and a metering chamber (32) may be sealed by either or both radial and flange seals or the like. In another embodiment, the present invention a seal may include a radial o-ring seal (21), a flange o-ring (22) and the like seals to create a seal between the reservoir and a metering chamber (32).

30

A reservoir may be interchangeable and disposable, in embodiments, or may even be refillable and re-useable, in other embodiments. Accordingly, a reservoir may include an interchangeable reservoir or may even include a refillable reservoir. In method

systems, the present invention may include interchanging a reservoir and may even include refilling a reservoir. An opening, such as a screw cap, snap or the like may be added to a reservoir in which liquid may be poured into the reservoir. In contrast, a reservoir may be pre-filled with liquid and when empty, a reservoir may be replaced with
5 a new pre-filled reservoir.

In embodiments, the present invention may include a liquid metering chamber that may accurately control an amount of fluid dispensed. An amount of fluid may be controlled by action of a diaphragm or other flexible element, which may be assembled
10 into a cavity of a dispenser housing (24). This may cause volumetric changes and may even create a metering chamber. A static seal may prevent leakage of fluids within a metering chamber and throughout a dispensing system. Action of a diaphragm may not be collinear or axially related to a liquid flow or reagent stream. A diaphragm action may be non-linear to a reagent stream. In other embodiments, a volume created by the
15 metering chamber may determine a volume of dispensed fluid.

In embodiments, a metering chamber may include an enclosed chamber or cavity that may have a flexible diaphragm (33). A flexible diaphragm may be displaced between compressed (37) and uncompressed positions (36), as seen in Figs. 7 and 8. By
20 compressed and uncompressed, it can be understood that a diaphragm may be a flexible membrane that can be displaced, bent, translated, conformed and the like. For example, a diaphragm may be placed in a compressed position (37) as seen in Fig. 8 or a diaphragm may be placed in an uncompressed position (36) as seen in Fig. 7. When a diaphragm is displaced from a free, extended or uncompressed position (36) to an
25 inverted or compressed position, it may substantially conform to an inner surface of a metering chamber. In a compressed position (37), a diaphragm may be capable of substantial conformation to at least part of a metering chamber. Specifically, in embodiments, a diaphragm may be capable of substantially conforming to a wall (15) of
metering chamber. By conformation and conforming, it is to be understood that at least
30 part of a diaphragm may become similar in form to an internal wall (15) of a metering chamber, such as seen in Fig. 8. In embodiments, a flexible diaphragm may be concave in its relaxed or uncompressed state and may be partially convex in its compressed state.

Opposite a metering chamber and attached to the dispenser housing (24) may be a unidirectional valve or the like element. At the bottom of the dispenser housing, a second unidirectional valve assembly, or the like element, may be attached. The assembly may utilize a disk that may even serve the dual purpose of a sealing surface and a flow director (19).

An inlet unidirectional valve (34) may connect a liquid introduction element (3) to a metering chamber and may provide an entrance for liquid into a metering chamber. An inlet unidirectional valve may open and close. When an inlet unidirectional valve is open, it may allow fluid to flow from a reservoir through a liquid introduction element and into a metering chamber. Contrarily, an inlet unidirectional valve may also prevent liquid from flowing into a metering chamber when it is closed. Liquid from a reservoir may flow through at least one liquid flow opening (7) and a membrane (8) of an inlet unidirectional valve (34). Of course, there may be other embodiments in which more than one liquid flow opening may be utilized, such as four or more liquid flow openings, and all are intended to be included in this disclosure. In an open position (9), an inlet unidirectional valve may have a membrane (8) positioned away from said liquid flow opening (7) so as to allow liquid to flow into a metering chamber. In a closed position (10), a membrane may close a liquid flow opening and even create a seal. In other embodiments, a positive seal may be formed in an inlet unidirectional valve.

In yet other embodiments, the present invention may provide a liquid flow deflection element (4) and may even provide deflectingly flowing an amount of liquid from a reservoir to a metering chamber through an inlet unidirectional valve. A liquid flow deflection element (4) may include a vertical flow element (12) below a reservoir and a horizontal flow element (13) next to a metering chamber. The present invention may include vertically flowing liquid out of a reservoir and horizontally flowing liquid into a metering chamber. To provide this, the present invention may include locating a reservoir somewhat above a metering chamber and locating an inlet unidirectional valve on a side (62) of a metering chamber as shown in Fig. 5. A vertical flow element (14) may be located below a metering chamber providing a vertically flowing liquid out of a metering chamber.

A diaphragm may be compressed and uncompressed with a plunger (23). A plunger (23) may be any structure and even a circular structure that may move a diaphragm. An actuator (16) may apply force to a plunger to move or even displace a diaphragm from one position to another. In embodiments, the present invention may provide horizontal displacement of a flexible diaphragm between compressed and uncompressed positions. This may include a substantially vertical diaphragm capable of moving in a horizontal direction. As such, in embodiments, a plunger may be configured to horizontally displace at least part of a metering chamber such as, a flexible diaphragm. In embodiments, the present invention may include a compression element and an uncompression element. A compression element may include a manual compression element or may even include an automatic compression element. Manual compression may include compression done or operated by a hand or hands rather than by an electrical or electronic device. Automatic compression may include compression that can be independently operated by an electronic device, such as but not limited to a stepper/servo control, a motor, an air cylinder or the like.

An uncompression element may include a force that can uncompress or displace a diaphragm to an uncompressed state. For example, an uncompression element may include a spring (40) which may be connected to a plunger (23). For clarity, a spring is not fully shown in the figures. The spring (40) apertures are meant to be representative of where a spring may be located. A force may be applied to a plunger which may compress a spring and displace a diaphragm. When this force is removed, a spring may uncompress and move a plunger along with a diaphragm in the opposite direction. In embodiments, a flexible diaphragm (33) may be displaced from a compressed position to an uncompressed position with a spring.

A liquid exit element (17) may be connected to a metering chamber and may even have an outlet unidirectional valve (25). In embodiments, the present invention may include distributing an amount of liquid from a metering chamber through an outlet unidirectional valve. A liquid exit element (17) may include a narrow channel (35) between a metering chamber and an outlet unidirectional valve (25). A lower or outlet unidirectional check valve assembly, as seen in Figs. 4 and 6, may attach to a dispenser housing (24). An outlet unidirectional valve (25) may only allow liquid to flow in one

direction and may include an open position (46) and a closed position (45). An outlet unidirectional valve may include at least one liquid flow opening and a membrane. In an open position (46), an outlet unidirectional valve may have a membrane positioned away from a liquid flow opening (20) so as to allow liquid to flow out of a metering chamber.

5 In a closed position (45), a membrane may close a liquid flow opening and even create a seal.

In some embodiments, an outlet unidirectional valve may include, but is not limited to, a valve disk (41), a valve retainer (42), and a valve membrane (43). A valve

10 retainer may form a seal between a valve membrane and a metering chamber. A valve disk may have a conical protrusion, a conical disk or other shape that may form a seal with a valve membrane. A valve membrane may be a flexible membrane. Of course, other shapes of disks are certainly possible. A valve disk may provide a seal surface and may even provide a flow director (19) which may direct a liquid flow through an outlet

15 unidirectional valve. A seal may be formed between a protrusion on a valve disk and an orifice on a valve membrane because the protrusion on a valve disk may deform a flexible valve membrane and may keep it under tension. In embodiments, an outlet unidirectional valve may be sealingly attached to a metering chamber and may even provide for positively sealingly attaching an outlet unidirectional valve to a metering

20 chamber. An elastic force of a valve membrane may provide a positive fluid seal for the dispenser assembly. Fluid pressure may separate a valve membrane from a valve disk during a dispense cycle and fluid may be expelled through an orifice in a valve membrane. A valve retainer may allow the attachment of a unidirectional valve assembly to a dispenser housing (24). Further, a seal may be located between the lower

25 valve retainer (42) and the dispenser housing (24). In an embodiment, a lower valve membrane (43) may be located near the lower valve disk (41).

The present invention may include a dual clamp element (26) as can be understood in Figs. 3, 11 and 12. The present invention may include clamping a

30 reservoir to a metering chamber and may even include attaching a reservoir and a metering chamber to an automated system. This may be provided with a dual clamp element (26) which may connect a liquid reservoir (11) to a metering chamber and may even connect or register a reservoir and metering chamber to an automated system. A

clamp may include, but is not limited to, a left clamp (27) and a right clamp (28) and may even include an automated system attachment (29), as seen in Figs. 3 and 12. The mechanism of attachment for the dispenser assembly and fluid reservoir may serve at least two purposes. It can clamp the liquid reservoir to the dispenser housing and may even provide a mounting feature for location on an automated system. Elastomeric o-rings or the like element may be used in either or both a radial and flange configuration at an interface between a liquid reservoir and a dispenser housing to prevent fluid leakage.

10 The present invention may include, in embodiments, creating a vacuum in a metering chamber. A vacuum may be an enclosed space from which matter, such as air, has been at least partially removed so that the matter or gas remaining in the space exerts less pressure than the atmosphere. When a metering chamber moves between compressed and uncompressed positions, a vacuum may be created as liquid is
15 dispensed. A vacuum created by the compression and release of a diaphragm may draw fluid from a reservoir into a metering chamber through an inlet unidirectional check valve. A precise volume of fluid may be drawn from a reservoir and dispensed from a metering chamber through an outlet unidirectional valve during a dispense cycle.

20 In embodiments, a liquid reservoir may include a collapsible molded reservoir (51) and even a collapsible plastic molded bottle, as shown in Fig. 2. A collapsible molded reservoir may include a single piece collapsible molded reservoir or a one piece structure. The material properties of a bottle may be highly compatible with most chemical and biological reagents. A collapsible molded reservoir may include a
25 chemically compatible material such as but not limited to polyolefin, inert materials, elastic materials and the like. A vacuum that may be built up inside a reservoir from the dispensing of fluid may not need to be released due to the fact that a reservoir may include a collapsible bottle. A vacuum may at least partially collapse a molded reservoir. The material and thickness of a bottle may be such that evaporation and permeability are
30 minimized while at the same time may even allow for a bottle to collapse due to the vacuum created from the withdrawal of fluid. It may be desirable, in embodiments, to provide balancing of a collapsibility of a collapsible molded reservoir with a durability of a collapsible molded reservoir.

In other embodiments, the present invention may include a collapsible molded reservoir (51) that may be a structured bottle which can yield to vacuum forces and yet substantially maintain its shape even when it is partially or fully collapsed. This may provide a reservoir or bottle that does not puncture and leak fluids. In embodiments, a molded reservoir may be made of a material that allows it to substantially maintain its structure. In embodiments, a reservoir may begin to collapse due to a vacuum in a metering chamber, and a reservoir may maintain or at least in part maintain its original shape or structure except for partial or even full indentation of the walls (60) of the reservoir, as may be shown in Figs. 13 and 14.

The forces required to collapse a bottle may be less and may even be significantly less than the forces required to displace a diaphragm. In embodiments, the present invention may include a reservoir collapse force less than a force required to uncompress a metering chamber and may even provide at least partially collapsing a collapsible molded reservoir with a force less than a force required to uncompress a metering chamber. A diaphragm can return to its uncompressed or free state with the assistance of an uncompression element, such as a spring or the like element.

In some embodiments, a diaphragm assembly may consist of at least a plastic molded diaphragm, a compression spring and a dispense plunger. A dispense plunger may be snapped onto a molded diaphragm. A material for a molded diaphragm may have similar properties as that described herein for a liquid reservoir. A diaphragm may be placed in a cavity in a dispenser housing forming a metering chamber. A diaphragm may form a static seal against a dispenser housing when a retainer, or the like element, and an elastomeric o-ring, or the like element, may be snapped into position against the outside of the diaphragm. Further, in embodiments, fluid may be moved through the metering chamber without any sliding parts. The fluid may simply be dispensed with non-sliding parts or may even be dispensed with reduced friction. Sliding parts may create friction, as it may be understood to occur in the syringe pump design. The disadvantages of syringe pump designs, such as the elastomer to chemical reagent incompatibility and elastomeric seal to syringe barrel tolerance concerns, may be eliminated since a fluid seal may be static in embodiments. Accordingly, the present

invention may include, in embodiments, a reduced friction dispenser and may even provide minimal sliding parts. The present invention reduces the amount of friction created and allows for conservation of energy.

5 To prime a metering chamber, a dispenser assembly may be compressed and released. Compression of a plunger may be accomplished by either manual method or automation methods. A user of the reagent cartridge could depress a plunger with a finger or thumb to prime the system initially. An automated system, as previously discussed, could use a number of devices to compress a plunger such as, but not limited to a stepper/servo motor, an air cylinder, or the like element. In embodiments, a dispenser assembly may be primed or used by compressing a plunger and releasing a plunger. This may be accomplished by manual operation or even by automated operation.

15 The present invention may include, in embodiments, tip-down priming a metering chamber with a tip-down priming element. Past attempts may have required a tip to be facing up so that air bubbles that may be trapped are released at the top. Air bubbles may be then evacuated by drawing them out with a syringe or other means. The use of an additional syringe may be both complicated and costly. Tip up priming may be inherently unsafe and can even require additional precautions to prevent harmful contact with the chemical being primed. The present invention may provide little or negligible amounts of air that can be trapped in a system. In embodiments, the shape of the diaphragm may match or even closely match the contour of the inner surface of the dispenser housing when the diaphragm is compressed using the method described above.

20 This design may force any trapped air through a narrow channel, which may be formed in the dispenser housing, and out of the lower unidirectional valve. A narrow channel may minimize a dead volume of reagent chemistry. Dead volume may be the volume that is not directly contained in the metering chamber and may not be expelled during the priming and/or normal dispense operation. A narrow channel may minimize the amounts of reagent or liquid not directly contained in the metering channel.

25

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In an embodiment, a vacuum created inside the metering chamber, when a diaphragm is returned to its free state or uncompressed position, may open up an upper

unidirectional valve. Fluid from a liquid reservoir (11) may flow into the metering chamber. A dispenser assembly (1) may be self-priming because there may be little dead-volume in the metering chamber and the shape of the cavity in the dispenser housing may closely match the shape of the diaphragm in the extended state.

5 Accordingly, the present invention may include, in embodiments, self priming a metering chamber and may even include a self priming element. A self priming element may include a flexible diaphragm and a metering chamber.

10 For each dispense cycle, an equal volume of fluid may be drawn from the reservoir and dispensed from the dispenser housing through the lower unidirectional check valve. A dispense cycle may be defined as one series of displacing a diaphragm to an extended state or compressed position and displacing a diaphragm in its free state or uncompressed position. A compression spring may overcome a vacuum formed inside the liquid reservoir to return the diaphragm to its free state or uncompressed position.

15 (36), as shown in Fig. 7. The accuracy and consistency of a dispensed fluid may be tightly controlled due to the fact that a metering chamber volume can remain the same. A spring can return a diaphragm to an internal mechanical stop (31) in its free state or uncompressed state and the compressed state of the diaphragm may be controlled by the inner surface of the dispenser housing. Accurate and repeatable dispense volume can be

20 critical for an automated system. The requirements and justification for an automatic system may be consistency across a multitude of tests and operations. The present invention may be less susceptible to variations and tolerances than other presently available dispensing apparatus utilizing the disposable dispensing assembly design approach.

25

In yet other embodiments, the present invention may provide for staining a biological sample with a distributed amount of liquid from a metering chamber. In order to achieve this, the present invention may provide a biological sample located directly below a liquid exit element. A biological sample may include tissues, cells, other

30 elements that may pertain to living organisms, or the like samples which may be desirable to process in a staining method. For example, but not limited to, staining methods and biological stains may include immunohistochemical stains, in Situ Hybridization, special stains or the like stains. In other embodiments, the present

invention may include an automated system for automated biological staining and may even use an automated system attachment as previously described.

5 The present invention may extend the usable shelf life of the chemistry stored in a liquid reservoir due to the fact that air may not be introduced into the system during the dispensing process and may even be a non-air exposing system. Other dispensing systems may require the release of vacuum, which is created as the fluid is evacuated from the reservoir. Further, other designs may utilize a valve or vented cap. A collapsible bottle design in embodiments of the present invention may not require air
10 introduction. In other embodiments, the present invention may provide limited light exposure. Some chemicals may be sensitive to light and may degrade with exposure to light. This may be accomplished by a reservoir housing which may keep light out of a reservoir and may even be accomplished by providing a non-light permeable structure for a metering chamber and the like.

15

In embodiments, the flexible liquid reservoir may be molded from a polyolefin material, or the like materials. Past attempts have utilized flexible liquid reservoirs made from a film material, which may then be manufactured into a bag. Bags may be manufactured using unreliable sealing methods to form a container. A seal formed
20 during the heat and compression manufacturing method can be susceptible to voids, holes, and non-uniformity. From one perspective, molding a flexible reservoir may be cost effective, reliable, and provide a uniform seal. Polyolefin material may be inert to most chemicals due to its homogeneity nature and material properties of polyolefin may also provide a modulus of elasticity that may minimize the forces required to collapse a
25 reservoir.

In other embodiments and as shown in Fig. 11, a reservoir housing (44) may be used to contain a reservoir and may even be attached around a reservoir. Reservoir housing (44) may include, but is not limited to, a left housing element (52) and a right
30 housing element (53), as shown in Fig. 3. Of course, a housing may be any number of pieces. A reservoir housing may provide a surface for identification by either an automated instrument or a user. It may also provide protection and support for a

reservoir. In an embodiment, the present invention may include a reservoir assembly in which the reagent may be contained.

5 In an embodiment, the end of travel for the diaphragm, which may be part of the metering chamber, may be controlled by a hard stop. This feature can eliminate the need for calibration of this assembly. Other designs may require the travel of the actuation device, for example, stepper/servo motors, air cylinders, and the like, to be calibrated to account for mechanical tolerances, which may be introduced as part of the assembly process. With this invention, a dispensed volume can remain consistent from position to position within an automated instrument or between multiple instruments. Dispense volume repeatability can be critical for consistent sample processing on the automated system.

15 In embodiments, the design of the metering chamber may allow for the use of a shipping lock. This feature may hold the diaphragm in a compressed position. A feature or element on the diaphragm may be positioned to contact the upper unidirectional valve and may prevent the flow of a liquid, such as a reagent, into the metering chamber. This unique and novel feature may serve two purposes. It may increase the shelf life of the product and it may prevent fluid from dripping during shipping. In embodiments, the present invention may include locking a metering chamber with a shipping lock to prevent liquid from flowing out of a reservoir. A shipping lock may hold a diaphragm in a compressed position to prevent liquid flow from a reservoir and a liquid introduction element from entering a metering chamber. A compressed position may further hold a inlet unidirectional valve in a closed position.

25 A flexible diaphragm (33) may be a single piece flexible diaphragm or even a one piece structure. In embodiments, a diaphragm may be plastic molded and may even be a flexible membrane. It may be desirable to provide a diaphragm that is made out of a chemically resistant material, such as a polyolefin material. A flexible diaphragm utilized in an embodiment of the present invention may be unique in that it may provide a flexible membrane that is chemically resistant and may also contain features to allow it to connect to the dispense plunger. Past attempts for flexible chemically resistant diaphragms may have been made from a sheet of plastic and may not adequately have

mounting features or may be made out of a plastic and rubber composite that may contain either an inserted plastic or metal feature to connect to the dispense mechanism.

Again, as mentioned earlier, in embodiments of the present invention, polyolefin material may be used and may be inert to most chemicals due to its homogeneity nature.

- 5 The material properties of the polyolefin material used for the manufacture of the diaphragm may also provide a modulus of elasticity that minimizes the forces required to compress it.

- 10 The present invention may include internally compressing a diaphragm with an internal diaphragm compressor. This may include compressing a diaphragm internally within a metering chamber structure wherein a plunger and diaphragm may be located within a structure, such as a metering chamber.

- 15 The present invention may include repeatably measuring an amount of liquid in a metering chamber. A metering chamber may include a repeatable liquid measurement element, which may provide measuring amounts of liquid accurately with each compression of a metering chamber. For example, a metering chamber may have a liquid measurement amount of about 250 microliters (μ l) which may be distributed from a metering chamber with each dispense stroke. A reagent pack or reservoir may be filled to about 120 milliliters (ml) for a total of one hundred, four stroke tests or a total of four hundred total dispenses. In embodiments, 20 milliliters (ml) may be used for priming. As but one additional example, a reservoir may include about 4 ml of fluid and a dispense amount may include about 500 micro liters. Of course, other dispense amounts and reservoir amounts are certainly possible and all are meant to be included in this disclosure.
- 20
- 25

- A volume of the dispensed amount may be defined by an inside cavity of a dispense chamber or metering chamber formed on one side by a diaphragm and on another side by a dispenser housing or a wall of a metering chamber. Each dispense stroke may be accurate for any type of liquid which may be dispensed. Of course, in embodiments, a dispenser assembly may not adequately dispense viscous liquids. A full stroke may dispense the entire liquid content inside a dispense chamber or metering chamber. To accurately measure each amount of liquid, the present invention may
- 30

include stopping a diaphragm in a metering chamber at an internal mechanical stop (31). An internal mechanical stop may stop displacement of a metering chamber or even a diaphragm at a uncompressed position.

5 Generally, a dispensing system may operate by displacing a diaphragm from a compressed position to an uncompressed position. A vacuum may be created which allows liquid to pass from a reservoir into a liquid introduction element and flow into a metering chamber through an open inlet unidirectional valve. An inlet unidirectional valve will open while an outlet unidirectional valve can close. When a metering
10 chamber may be full, a diaphragm may begin to move from an uncompressed position to a compressed position. An inlet unidirectional valve may close and an outlet unidirectional valve may open allowing the measured liquid to flow out of a metering chamber through an exit element.

15 In Fig. 9, an embodiment of a dispenser system is shown when a plunger and diaphragm may be moving from a compressed state to a free or uncompressed state by action of an internal spring. In this diagram, an outlet unidirectional valve may be closed and an inlet unidirectional valve may be open. This may allow fluid to enter a metering chamber from a collapsible fluid reservoir. In this situation, vacuum builds which may
20 close an outlet unidirectional valve immediately and may open an inlet unidirectional valve or umbrella valve once the "cracking pressure" has been reached.

 Fig. 10 shows an embodiment of a dispenser system when a plunger and diaphragm may be moving from a free or uncompressed position to a compressed
25 position as it is being actuated by a staining instrument. In this figure, an inlet unidirectional valve or even an umbrella may be closed and an output unidirectional valve may be open. This may allow fluid to exit a metering chamber and dispense onto test samples. In this situation, pressure may build inside a metering chamber. A pressure may immediately close an inlet unidirectional valve and can open an outlet
30 unidirectional valve once a "cracking pressure" or an opening pressure of an outlet unidirectional valve has been reached.

As can be easily understood from the foregoing, the basic concepts of the present invention may be embodied in a variety of ways. It involves both dispensing techniques as well as devices to accomplish the appropriate dispenser. In this application, the dispensing techniques are disclosed as part of the results shown to be achieved by the various devices described and as steps which are inherent to utilization. They are simply the natural result of utilizing the devices as intended and described. In addition, while some devices are disclosed, it should be understood that these not only accomplish certain methods but also can be varied in a number of ways. Importantly, as to all of the foregoing, all of these facets should be understood to be encompassed by this disclosure.

The discussion included in this application is intended to serve as a basic description. The reader should be aware that the specific discussion may not explicitly describe all embodiments possible; many alternatives are implicit. It also may not fully explain the generic nature of the invention and may not explicitly show how each feature or element can actually be representative of a broader function or of a great variety of alternative or equivalent elements. Again, these are implicitly included in this disclosure. Where the invention is described in device-oriented terminology, each element of the device implicitly performs a function. Apparatus claims may not only be included for the device described, but also method or process claims may be included to address the functions the invention and each element performs. Neither the description nor the terminology is intended to limit the scope of the claims which will be included in any subsequent patent application.

It should also be understood that a variety of changes may be made without departing from the essence of the invention. Such changes are also implicitly included in the description. They still fall within the scope of this invention. A broad disclosure encompassing both the explicit embodiment(s) shown, the great variety of implicit alternative embodiments, and the broad methods or processes and the like are encompassed by this disclosure and may be relied upon when drafting the claims for any subsequent patent application. It should be understood that such language changes and broader or more detailed claiming may be accomplished at a later date or in the event the applicant subsequently seeks a patent filing based on this filing. With this understanding, the reader should be aware that this disclosure is to be understood to

support any subsequently filed patent application that may seek examination of as broad a base of claims as deemed within the applicant's right and may be designed to yield a patent covering numerous aspects of the invention both independently and as an overall system.

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Further, each of the various elements of the invention and claims may also be achieved in a variety of manners. This disclosure should be understood to encompass each such variation, be it a variation of an embodiment of any apparatus embodiment, a method or process embodiment, or even merely a variation of any element of these. Particularly, it should be understood that as the disclosure relates to elements of the invention, the words for each element may be expressed by equivalent apparatus terms or method terms -- even if only the function or result is the same. Such equivalent, broader, or even more generic terms should be considered to be encompassed in the description of each element or action. Such terms can be substituted where desired to make explicit the implicitly broad coverage to which this invention is entitled. As but one example, it should be understood that all actions may be expressed as a means for taking that action or as an element which causes that action. Similarly, each physical element disclosed should be understood to encompass a disclosure of the action which that physical element facilitates. Regarding this last aspect, as but one example, the disclosure of a "dispenser" should be understood to encompass disclosure of the act of "dispensing" -- whether explicitly discussed or not -- and, conversely, were there effectively disclosure of the act of "dispensing", such a disclosure should be understood to encompass disclosure of a "dispensing" and even a "means for dispensing". Such changes and alternative terms are to be understood to be explicitly included in the description.

25

U.S. PATENT DOCUMENTS

DOCUMENT NO.	DATE	NAME	CLASS	SUB CLASS	FILING DATE
4,844,868	7/4/1989	Rokugawa	422	64	6/11/1986
5,232,664	8/3/1993	Krawzak et al.	422	64	9/18/1991
5,316,452	5/31/1994	Bogen et al.	417	412	5/11/1992
5,634,391	6/3/1997	Eady	92	97	7/09/1996
5,645,114	7/8/1997	Bogen et al.	141	145	5/31/1994

5,947,167	9/7/1999	Bogen et al.	141	1	7/02/1997
6,045,759	4/4/2000	Ford et al.	422	103	12/19/1997
6,092,695	7/25/2000	Loeffler	222	207	2/10/1998
6,183,693	2/6/2001	Bogen et al.	422	64	02/27/1998
6,180,061	1/30/2001	Bogen et al.	422	64	12/04/1998
6,244,474	6/12/2001	Loeffler	222	207	7/6/2000

All patents, publications, or other references mentioned in this application for
 patent or listed in the above listing are hereby incorporated by reference. The priority
 5 case, United States of America Provisional Application No. 60/477,382, filed 09 June
 2003, is hereby incorporated by reference including any figures or attachments. In
 addition, as to each term used it should be understood that unless its utilization in this
 application is inconsistent with such interpretation, common dictionary definitions
 should be understood as incorporated for each term and all definitions, alternative terms,
 10 and synonyms such as contained in the Random House Webster's Unabridged
 Dictionary, second edition are hereby incorporated by reference. Finally, all references
 listed herein or other information statement filed with the application are hereby
 appended and hereby incorporated by reference, however, as to each of the above, to the
 extent that such information or statements incorporated by reference might be considered
 15 inconsistent with the patenting of this/these invention(s) such statements are expressly
 not to be considered as made by the applicant(s).

Thus, the applicant(s) should be understood to have support to claim and make a
 statement of invention to at least: i) each of the dispenser devices as herein disclosed and
 20 described, ii) the related methods disclosed and described, iii) similar, equivalent, and
 even implicit variations of each of these devices and methods, iv) those alternative
 designs which accomplish each of the functions shown as are disclosed and described, v)
 those alternative designs and methods which accomplish each of the functions shown as
 are implicit to accomplish that which is disclosed and described, vi) each feature,
 25 component, and step shown as separate and independent inventions, vii) the applications
 enhanced by the various systems or components disclosed, viii) the resulting products
 produced by such systems or components, ix) each system, method, and element shown

or described as now applied to any specific field or devices mentioned, x) methods and apparatuses substantially as described hereinbefore and with reference to any of the accompanying examples, xi) the various combinations and permutations of each of the elements disclosed, and xii) each potentially dependent claim or concept as a dependency
5 on each and every one of the independent claims or concepts presented.

With regard to claims whether now or later presented for examination, it should be understood that for practical reasons and so as to avoid great expansion of the examination burden, the applicant may at any time present only initial claims or perhaps
10 only initial claims with only initial dependencies. Support should be understood to exist to the degree required under new matter laws -- including but not limited to European Patent Convention Article 123(2) and United States Patent Law 35 USC § 132 or other such laws-- to permit the addition of any of the various dependencies or other elements presented under one independent claim or concept as dependencies or elements under
15 any other independent claim or concept. In drafting any claims at any time whether in this application or in any subsequent application, it should also be understood that the applicant has intended to capture as full and broad a scope of coverage as legally available. To the extent that insubstantial substitutes are made, to the extent that the applicant did not in fact draft any claim so as to literally encompass any particular
20 embodiment, and to the extent otherwise applicable, the applicant should not be understood to have in any way intended to or actually relinquished such coverage as the applicant simply may not have been able to anticipate all eventualities; one skilled in the art, should not be reasonably expected to have drafted a claim that would have literally encompassed such alternative embodiments.

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Further, if or when used, the use of the transitional phrase "comprising" is used to maintain the "open-end" claims herein, according to traditional claim interpretation. Thus, unless the context requires otherwise, it should be understood that the term "comprise" or variations such as "comprises" or "comprising", are intended to imply the
30 inclusion of a stated element or step or group of elements or steps but not the exclusion of any other element or step or group of elements or steps. Such terms should be interpreted in their most expansive form so as to afford the applicant the broadest coverage legally permissible.

Finally, any claims set forth at any time are hereby incorporated by reference as part of this description of the invention, and the applicant expressly reserves the right to use all of or a portion of such incorporated content of such claims as additional
5 description to support any of or all of the claims or any element or component thereof, and the applicant further expressly reserves the right to move any portion of or all of the incorporated content of such claims or any element or component thereof from the description into the claims or vice-versa as necessary to define the matter for which protection is sought by this application or by any subsequent continuation, division, or
10 continuation-in-part application thereof, or to obtain any benefit of, reduction in fees pursuant to, or to comply with the patent laws, rules, or regulations of any country or treaty, and such content incorporated by reference shall survive during the entire pendency of this application including any subsequent continuation, division, or continuation-in-part application thereof or any reissue or extension thereon.

15

VI. CLAIMS

1. A liquid dispenser apparatus comprising:
 - 5 a collapsible molded reservoir;
a compressible metering chamber fluidly connected to said collapsible molded reservoir with a liquid introduction element;
a liquid flow deflection element;
an inlet unidirectional valve which connects said liquid introduction element to a
10 metering chamber;
a flexible diaphragm capable of substantial conformation to at least part of said metering chamber;
a plunger configured to horizontally displace said flexible diaphragm; and
a liquid exit element connected to said metering chamber having an outlet unidirectional
15 valve.
2. A liquid dispenser apparatus comprising:
 - a liquid reservoir;
a compressible metering chamber fluidly connected to said liquid reservoir with a liquid
20 introduction element;
a liquid flow deflection element;
an inlet unidirectional valve which connects said liquid introduction element to said compressible metering chamber;
a plunger configured to horizontally displace at least part of said compressible metering
25 chamber; and
a liquid exit element connected to said metering chamber having an outlet unidirectional valve.
3. A liquid dispenser apparatus according to claim 2 wherein said inlet
30 unidirectional valve is located on a side of said metering chamber.

4. A liquid dispenser apparatus according to claim 2 said liquid flow deflection element comprises a vertical flow element below said reservoir and a horizontal flow element next to said metering chamber.
5. A liquid dispenser apparatus according to claim 4 and further comprising a vertical flow element below said metering chamber.
6. A liquid dispenser apparatus according to claim 2 wherein said compressible metering chamber comprises a flexible diaphragm.
- 10 7. A liquid dispenser apparatus comprising:
a liquid reservoir;
a metering chamber fluidly connected to said liquid reservoir with a liquid introduction element;
15 an inlet unidirectional valve which connects said liquid introduction element to a metering chamber;
a flexible diaphragm capable of substantial conformation to at least part of said metering chamber;
a plunger configured to compress and decompress said flexible diaphragm; and
20 a liquid exit element connected to said metering chamber having an outlet unidirectional valve.
8. A liquid dispenser apparatus according to claim 7 wherein said flexible diaphragm comprises a one piece diaphragm.
- 25 9. A liquid dispenser apparatus according to claim 7 wherein said flexible diaphragm comprises a polyolefin material.
10. A liquid dispenser apparatus according to claim 7 wherein said flexible
30 diaphragm capable of substantial conformation to at least part of said metering chamber comprises a flexible diaphragm capable of substantial conformation to a wall of said metering chamber.

11. A liquid dispenser apparatus comprising:
a collapsible molded reservoir;
a compressible metering chamber fluidly connected to said liquid reservoir with a liquid introduction element;
- 5 an inlet unidirectional valve which connects said liquid introduction element to said compressible metering chamber;
a plunger configured to displace at least part of said compressible metering chamber; and
a liquid exit element connected to said metering chamber having an outlet unidirectional valve.
- 10 12. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said reservoir comprises a one piece structure.
13. A liquid dispenser apparatus according to claim 11 wherein said collapsible
15 molded reservoir comprises a structured bottle.
14. A liquid dispenser apparatus according to claim 11 and further comprising a reservoir collapse force less than a force required to uncompress said metering chamber.
- 20 15. A liquid dispenser apparatus according to claim 11 wherein said reservoir comprises an interchangeable reservoir.
16. A liquid dispenser apparatus according to claim 11 wherein said reservoir
25 comprises a refillable reservoir.
17. A liquid dispenser apparatus according to claim 7 or 11 and further comprising a liquid flow deflection element.
18. A liquid dispenser apparatus according to claim 17 wherein said inlet
30 unidirectional valve is located on a side of said metering chamber.

19. A liquid dispenser apparatus according to claim 17 wherein said liquid flow deflection element comprises a vertical flow element below said reservoir and a horizontal flow element next to said metering chamber.
- 5 20. A liquid dispenser apparatus according to claim 19 and further comprising a vertical flow element below said metering chamber.
21. A liquid dispenser apparatus according to claim 1 wherein said inlet unidirectional valve is located on a side of said metering chamber.
- 10 22. A liquid dispenser apparatus according to claim 1 wherein said liquid flow deflection element comprises a vertical flow element below said reservoir and a horizontal flow element next to said metering chamber.
- 15 23. A liquid dispenser apparatus according to claim 22 and further comprising a vertical flow element below said metering chamber.
24. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a dual clamp element.
- 20 25. A liquid dispenser apparatus according to claim 24 wherein said dual clamp element connects said liquid reservoir to said metering chamber and wherein said dual clamp connects said connected reservoir and metering chamber to an automated system.
- 25 26. A liquid dispenser apparatus according to claim 24 wherein said dual clamp element comprises a left clamp and right clamp.
27. A liquid dispenser apparatus according to claim 24 wherein said dual clamp element comprises an automated system attachment.
- 30 28. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a biological sample located directly below said liquid exit element.

29. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising an automated biological staining device.
30. A liquid dispenser apparatus according to claim 29 wherein said automated
5 biological staining device comprises a biological stain selected from a group consisting of a immunohistochemical staining device, special stains staining device, and an in situ hybridization device.
31. A liquid dispenser apparatus according to claim 11 wherein said compressible
10 metering chamber comprises a flexible diaphragm.
32. A liquid dispenser apparatus according to claim 1 or 7 and further comprising an internal diaphragm compressor.
33. A liquid dispenser apparatus according to claim 6 or 31 and further comprising an
15 internal diaphragm compressor.
34. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said
metering chamber comprises a repeatable liquid measurement element.
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35. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said
metering chamber comprises a liquid measurement amount of about 250 micro liters.
36. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further
25 comprising an internal mechanical stop located in said metering chamber to stop displacement of said metering chamber at an uncompressed position.
37. A liquid dispenser apparatus according to claim 1, 6, 7 or 31 wherein said
flexible diaphragm comprises an uncompressed position and a compressed position.
30
38. A liquid dispenser apparatus according to claim 1, 6, 7 or 31 wherein said
flexible diaphragm comprises a plastic molded diaphragm.

39. A liquid dispenser apparatus according to claim 1, 6, 7 or 31 wherein said flexible diaphragm comprises a flexible membrane.
40. A liquid dispenser apparatus according to claim 1, 6, 7 or 31 wherein said
5 flexible diaphragm comprises a chemically resistant material.
41. A liquid dispenser apparatus according to claim 1, 6, 7 or 31 wherein said flexible diaphragm comprises a polyolefin material.
- 10 42. A liquid dispenser apparatus according to claim 1, 6, 7 or 31 wherein said flexible diaphragm comprises a one piece diaphragm.
43. A liquid dispenser apparatus according to claim 37 wherein said compressed position comprises said diaphragm substantially conformed to a shape of at least part of
15 said metering chamber.
44. A liquid dispenser apparatus according to claim 2 or 11 and further comprising a plunger to which said compressible metering chamber is responsive.
- 20 45. A liquid dispenser apparatus according to claim 1 or 7 and further comprising an actuator to which said plunger and said flexible diaphragm is responsive.
46. A liquid dispenser apparatus according to claim 2 or 11 and further comprising an actuator to which said plunger and said compressible metering chamber is responsive
25
47. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a compression element and a uncompression element.
48. A liquid dispenser apparatus according to claim 47 wherein said uncompression
30 element comprises a spring.
49. A liquid dispenser apparatus according to claim 47 wherein said compression element comprises a manual compression element.

50. A liquid dispenser apparatus according to claim 47 wherein said compression element comprises an automatic compression element.
- 5 51. A liquid dispenser apparatus according to claim 50 wherein said automatic compression element comprises compression selected from a group consisting of a stepper/servomotor control, a motor and an air cylinder.
52. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said outlet
10 unidirectional valve comprises:
a valve disk;
a valve retainer; and
a valve membrane.
- 15 53. A liquid dispenser apparatus according to claim 52 wherein said valve disk comprises a seal surface and a flow director.
54. A liquid dispenser apparatus according to claim 52 wherein said valve membrane
20 comprises flexible membrane.
55. A liquid dispenser apparatus according to claim 52 wherein said valve disk comprises conical disk.
56. A liquid dispenser apparatus according to claim 52 wherein said valve disk and
25 membrane comprises a seal.
57. A liquid dispenser apparatus according to claim 56 wherein said seal comprises a positive fluid seal.
- 30 58. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said outlet unidirectional valve comprises an open position and a closed position.

59. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a seal between said reservoir and said liquid introduction element.
60. A liquid dispenser apparatus according to claim 59 wherein said seal is selected
5 from a group consisting of a radial o-ring and flange o-ring.
61. A liquid dispenser apparatus according to claim 2 or 7 wherein said reservoir comprises a collapsible molded reservoir.
- 10 62. A liquid dispenser apparatus according to claim 61 wherein said collapsible molded reservoir comprises a structured bottle.
63. A liquid dispenser apparatus according to claim 1 wherein said collapsible molded reservoir comprises a structured bottle.
15
64. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said reservoir comprises a chemically compatible material.
65. A liquid dispenser apparatus according to claim 64 wherein said chemically
20 compatible material is selected from a group consisting of polyolefin, inert materials and elastic materials.
66. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising reservoir housing around said reservoir.
25
67. A liquid dispenser apparatus according to claim 66 wherein said reservoir housing comprises a left and right housing element.
68. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said liquid
30 exit element comprises a narrow channel between said metering chamber and said outlet unidirectional valve.

69. A liquid dispenser apparatus according to claim 7 wherein said reservoir comprises a collapsible molded reservoir and further comprising a reservoir collapse force less than a force required to uncompress said diaphragm.
- 5 70. A liquid dispenser apparatus according to claim 1 and further comprising a reservoir collapse force less than a force required to uncompress said diaphragm.
71. A liquid dispenser apparatus according to claim 2 wherein said reservoir comprises a collapsible molded reservoir and further comprising a reservoir collapse
10 force less than a force required to uncompress said metering chamber.
72. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said reservoir is located above said metering chamber.
- 15 73. A liquid dispenser apparatus according to claim 1, 2 or 7 wherein said reservoir comprises an interchangeable reservoir.
74. A liquid dispenser apparatus according to claim 1, 2 or 7 wherein said reservoir comprises a refillable reservoir.
20
75. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a reduced friction dispenser.
76. A liquid dispenser apparatus according to claim 75 wherein said reduced friction
25 dispenser comprises minimal sliding parts.
77. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a sealed system.
- 30 78. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a self priming element.

79. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further comprising a tip-down priming element.
80. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 and further
5 comprising a shipping lock.
81. A liquid dispenser apparatus according to claim 80 wherein said shipping lock comprises a diaphragm held in a compressed position to prevent liquid flow from said reservoir and said liquid introduction element.
- 10 82. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said liquid introduction element comprises a channel between said reservoir and said inlet unidirectional valve.
- 15 83. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said inlet unidirectional valve comprises at least one liquid flow opening and a membrane.
84. A liquid dispenser apparatus according to claim 83 wherein said membrane comprises a seal.
- 20 85. A liquid dispenser apparatus according to claim 84 wherein said seal comprises a positive seal.
86. A liquid dispenser apparatus according to claim 1, 2, 7 or 11 wherein said inlet
25 unidirectional valve comprises an open position and a closed position.
87. A liquid dispenser apparatus according to claim 7 wherein said plunger is configured to horizontally displace said diaphragm.
- 30 88. A liquid dispenser apparatus according to claim 11 wherein said plunger configured to displace at least part of said compressible metering chamber comprises a plunger configured to horizontally displace at least part of said metering chamber.

89. A liquid dispenser apparatus according to claim 1, 2, 87 or 88 wherein said plunger configured to horizontally displace comprises a substantially vertical diaphragm capable of moving in a horizontal direction.

- 5 90. A method of dispensing liquid comprising the steps of:
establishing liquid in a collapsible molded reservoir;
providing a metering chamber having a flexible diaphragm;
horizontally displacing said flexible diaphragm from a compressed position to an
uncompressed position;
10 creating a vacuum in said metering chamber;
opening an inlet unidirectional valve which allows liquid to flow from said reservoir to
said metering chamber;
deflectingly flowing an amount of liquid from said reservoir to said metering chamber
through said inlet unidirectional valve;
15 at least partially collapsing said molded reservoir with said vacuum;
substantially maintaining structure of said reservoir;
horizontally displacing said flexible diaphragm from said uncompressed position to said
compressed position;
closing said inlet unidirectional valve;
20 opening an outlet unidirectional valve;
substantially conforming said diaphragm against a wall of said metering chamber;
distributing said amount of liquid from said metering chamber through said outlet
unidirectional valve; and
closing said outlet unidirectional valve.

- 25 91. A method of dispensing liquid comprising the steps of:
establishing liquid in a reservoir;
providing a compressible metering chamber;
horizontally displacing at least part of said compressible metering chamber from a
compressed position to an uncompressed position;
30 opening an inlet unidirectional valve which allows liquid to flow from said reservoir to
said metering chamber;

deflectingly flowing an amount of liquid from said reservoir to said metering chamber through said inlet unidirectional valve;

horizontally displacing at least part of said compressible metering chamber from said uncompressed position to said compressed position;

5 closing said inlet unidirectional valve;

opening an outlet unidirectional valve;

distributing said amount of liquid from said metering chamber through said outlet unidirectional valve; and

closing said outlet unidirectional valve.

10

92. A method of dispensing liquid according to claim 91 and further comprising the step of locating said inlet unidirectional valve on a side of said metering chamber.

93. A method of dispensing liquid according to claim 91 wherein said step of
15 deflectingly flowing an amount of liquid from said reservoir to said metering chamber through said inlet unidirectional valve comprises the step of vertically flowing said liquid out of said reservoir and horizontally flowing said liquid into said metering chamber.

94. A method of dispensing liquid according to claim 93 and further comprising the
20 step of vertically flowing said liquid out of said metering chamber.

95. A method of dispensing liquid according to claim 91 wherein said step of horizontally displacing at least part of said compressible metering chamber from said uncompressed position to said compressed position comprises the step of horizontally
25 displacing a flexible diaphragm from an uncompressed position to a compressed position.

96. A method of dispensing liquid comprising the steps of:
establishing liquid in a reservoir;
30 providing a metering chamber having a flexible diaphragm;
displacing said flexible diaphragm from a compressed position to an uncompressed position;

- opening an inlet unidirectional valve which allows liquid to flow from said reservoir to said metering chamber;
flowing an amount of liquid from said reservoir to said metering chamber through said inlet unidirectional valve;
5 displacing said uncompressed diaphragm to a compressed position;
closing said inlet unidirectional valve;
opening an outlet unidirectional valve;
substantially conforming said diaphragm against at least part of said metering chamber;
distributing said amount of liquid from said metering chamber through said outlet
10 unidirectional valve; and
closing said liquid output unidirectional valve.

97. A method of dispensing liquid according to claim 96 wherein said step of providing a metering chamber having a flexible diaphragm comprises the step of
15 providing a metering chamber having a single piece flexible diaphragm.

98. A method of dispensing liquid according to claim 96 wherein said step of providing a metering chamber having a flexible diaphragm comprises the step of providing a polyolefin flexible diaphragm.
20

99. A method of dispensing liquid comprising the steps of
establishing liquid in a collapsible molded reservoir;
providing a compressible metering chamber;
displacing at least part of said metering chamber from a compressed position to an
25 uncompressed position;
opening an inlet unidirectional valve which allows liquid to flow from said reservoir to said metering chamber;
creating a vacuum in said metering chamber;
flowing an amount of liquid from said reservoir to said metering chamber through said
30 inlet unidirectional valve;
at least partially collapsing said molded reservoir with said vacuum;
substantially maintaining structure of said molded reservoir;

- displacing at least part of said metering chamber from said uncompressed position to said compressed position;
closing said inlet unidirectional valve;
opening an outlet unidirectional valve;
5 distributing said amount of liquid from said metering chamber through said outlet unidirectional valve; and
closing said outlet unidirectional valve.

100. A method of dispensing liquid according to claim 90, 91, 96 or 99 wherein said
10 step of establishing liquid in a reservoir comprises the step of establishing liquid in a single piece collapsible molded reservoir.

101. A method of dispensing liquid according to claim 99 wherein said step of
establishing liquid in a collapsible molded reservoir comprises the step of establishing
15 liquid in a structured collapsible molded reservoir.

102. A method of dispensing liquid according to claim 99 and further comprising the
step of at least partially collapsing said collapsible molded reservoir with a force less
than a force required to uncompress said metering chamber.
20

103. A method of dispensing liquid according to claim 99 and further comprising the
step of interchanging said collapsible molded reservoir.

104. A method of dispensing liquid according to claim 99 and further comprising the
25 step of refilling said collapsible molded reservoir.

105. A method of dispensing liquid according to claim 99 and further comprising the
step of balancing collapsibility of said collapsible molded reservoir with durability of
said collapsible molded reservoir.
30

106. A method of dispensing liquid according to claim 96 or 99 and further
comprising deflectingly flowing an amount of liquid from said reservoir to said metering
chamber through said inlet unidirectional valve.

107. A method of dispensing liquid according to claim 106 and further comprising locating said inlet unidirectional valve on a side of said metering chamber.
- 5 108. A method of dispensing liquid according to claim 106 wherein said step of deflectingly flowing an amount of liquid from said reservoir to said metering chamber through said inlet unidirectional valve comprises the step of vertically flowing said liquid out of said reservoir and horizontally flowing said liquid into said metering chamber.
- 10 109. A method of dispensing liquid according to claim 108 and further comprising vertically flowing said liquid out of said metering chamber.
110. A method of dispensing liquid according to claim 90 and further comprising locating said inlet unidirectional valve on a side of said metering chamber
- 15 111. A method of dispensing liquid according to claim 90 wherein said step of deflectingly flowing an amount of liquid from said reservoir to said metering chamber through said inlet unidirectional valve comprises the step of vertically flowing said liquid out of said reservoir and horizontally flowing said liquid into said metering chamber.
- 20 112. A method of dispensing liquid according to claim 111 and further comprising the step of vertically flowing said liquid out of said metering chamber.
113. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further
- 25 comprising the step of clamping said reservoir to said metering chamber.
114. A method of dispensing liquid according to claim 113 and further comprising the step of attaching said reservoir and said metering chamber to an automated system.
- 30 115. A method of dispensing liquid according to claim 113 wherein said step of clamping said reservoir to said metering chamber comprises the step of clamping said reservoir to said metering chamber with a left clamp and a right clamp.

116. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of staining a biological sample with said distributed amount of liquid.
- 5 117. A method of dispensing liquid according to claim 116 wherein said step of staining a biological sample with said distributed amount of liquid comprises the step of selecting a staining method from a group consisting of special stains, immunohistochemical stains, and in Situ Hybridization.
- 10 118. A method of dispensing liquid according to claim 117 and further comprising the step of automating said staining method.
119. A method of dispensing liquid according to claim 99 wherein said step of providing said compressible metering chamber comprises the step of providing a
15 metering chamber having a flexible diaphragm.
120. A method of dispensing liquid according to claim 95 or 119 and further comprising the step of substantially conforming said diaphragm against at least part of said metering chamber.
20
121. A method of dispensing liquid according to claim 120 wherein said step of substantially conforming said diaphragm against at least part of said metering chamber comprises the step of substantially conforming said diaphragm against a wall of said metering chamber.
25
122. A method of dispensing liquid according to claim 90 or 96 and further comprising the step of internally compressing said diaphragm.
123. A method of dispensing liquid according to claim 95 or 119 and further
30 comprising the step of internally compressing said diaphragm.
124. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising repeatably measuring an amount of liquid in said metering chamber.

125. A method of dispensing liquid according to claim 90, 91, 96 or 99 wherein said step of distributing said amount of liquid comprises the step of distributing about 250 micro liters of said liquid.
- 5
126. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of stopping said diaphragm in said metering chamber at an internal mechanical stop.
- 10
127. A method of dispensing liquid according to claim 90, 95, 96 or 119 wherein said step of providing a metering chamber having a flexible diaphragm comprises the step of providing a plastic molded diaphragm.
128. A method of dispensing liquid according to claim 90, 95, 96 or 119 wherein said
- 15 step of providing a metering chamber having a flexible diaphragm comprises the step of providing a metering chamber having a flexible membrane.
129. A method of dispensing liquid according to claim 90, 95, 96 or 119 wherein said
- 20 step of providing a metering chamber having a flexible diaphragm comprises the step of providing a chemically resistant diaphragm.
130. A method of dispensing liquid according to claim 90, 95 or 119 wherein said step of providing a metering chamber having a flexible diaphragm comprises the step of providing a polyolefin flexible diaphragm.
- 25
131. A method of dispensing liquid according to claim 90, 95 or 119 wherein said step of providing a metering chamber having a flexible diaphragm comprises the step of providing a metering chamber having a single piece flexible diaphragm.
- 30
132. A method of dispensing liquid according to claim 90 wherein said step of horizontally displacing said flexible diaphragm from a compressed position to an uncompressed position comprises the step of horizontally displacing said flexible diaphragm from a compressed position to an uncompressed position with a spring.

133. A method of dispensing liquid according to claim 91 wherein said step of horizontally displacing said at least part of said compressible metering chamber from a compressed position to an uncompressed position comprises the step of horizontally displacing said at least part of said compressible metering chamber from a compressed position to an uncompressed position with a spring.

134. A method of dispensing liquid according to claim 96 wherein said step of displacing said flexible diaphragm from a compressed position to an uncompressed position comprises the step of displacing said flexible diaphragm from a compressed position to an uncompressed position with a spring.

135. A method of dispensing liquid according to claim 99 wherein said step of displacing at least part of said compressible metering chamber from a compressed position to an uncompressed position comprises the step of displacing at least part of said compressible metering chamber from a compressed position to an uncompressed position with a spring.

136. A method of dispensing liquid according to claim 90 or 96 and further comprising manually compressing said flexible diaphragm.

137. A method of dispensing liquid according to claim 91 or 99 and further comprising manually compressing said compressible metering chamber.

138. A method of dispensing liquid according to claim 90 or 96 and further comprising automatically compressing said flexible diaphragm.

139. A method of dispensing liquid according to claim 91 or 99 and further comprising automatically compressing said compressible metering chamber.

140. A method of dispensing liquid according to claim 138 wherein said step of automatically compressing said flexible diaphragm comprises the step of compressing

with an a compression element selected from a group consisting of a stepper/servor control, a motor and an air cylinder.

5 141. A method of dispensing liquid according to claim 139 wherein said step of automatically compressing said flexible diaphragm comprises the step of compressing with an a compression element selected from a group consisting of a stepper/servor control, a motor and an air cylinder.

10 142. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of directing liquid flow through said outlet unidirectional valve.

15 143. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of sealingly attaching said outlet unidirectional valve to said metering chamber.

20 144. A method of dispensing liquid according to claim 143 wherein said step of sealingly attaching said outlet unidirectional valve to said metering chamber comprises the step of positively sealingly attaching said outlet unidirectional valve to said metering chamber.

25 145. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of sealingly attaching said reservoir to said metering chamber.

30 146. A method of dispensing liquid according to claim 145 wherein said step of sealingly attaching said reservoir to said metering chamber comprises the step of selecting a seal from a group consisting of a radial o-ring and a flange o-ring.

147. A method of dispensing liquid according to claim 91 or 96 wherein said step of establishing liquid in a reservoir comprises the step of establishing liquid in a collapsible molded reservoir.

148. A method of dispensing liquid according to claim 90, 91, 96 or 99 wherein said step of establishing liquid in said reservoir comprises the step of providing a chemically compatible reservoir.
- 5 149. A method of dispensing liquid according to claim 148 wherein said chemically compatible reservoir has a material selected from a group consisting of polyolefin, inert materials and elastic materials.
- 10 150. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising attaching reservoir housing around said reservoir.
- 15 151. A method of dispensing liquid according to claim 150 wherein said step of attaching said reservoir housing around said reservoir comprises the step of attaching a left housing element and right housing element.
152. A method of dispensing liquid according to claim 91 or 96 and further comprising the step of creating a vacuum.
- 20 153. A method of dispensing liquid according to claim 152 and further comprising the step of at least partially collapsing said reservoir with a force less than a force required to uncompress said metering chamber.
- 25 154. A method of dispensing liquid according to claim 90 and further comprising the step of at least partially collapsing said collapsible molded reservoir with a force less than a force required to uncompress said diaphragm.
- 30 155. A method of dispensing liquid according to claim 90 or 147 and further comprising the step of balancing collapsibility of said collapsible molded reservoir with durability of said collapsible molded reservoir.
156. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of locating said reservoir above said metering chamber.

157. A method of dispensing liquid according to claim 90, 91 or 96 and further comprising the step of interchanging said reservoir.
158. A method of dispensing liquid according to claim 90, 91 or 96 and further
5 comprising the step of refilling said reservoir.
159. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of utilizing minimally sliding parts in said dispensing system.
- 10 160. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of self priming said metering chamber.
161. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of tip-down priming said metering chamber.
15
162. A method of dispensing liquid according to claim 90, 91, 96 or 99 and further comprising the step of locking said metering chamber to prevent liquid from flowing from said reservoir.
- 20 163. A method of dispensing liquid according to claim 162 wherein said step of locking said metering chamber to prevent liquid from flowing from said reservoir comprises the step of holding a diaphragm in a compressed position.
164. A method of dispensing liquid according to claim 90, 91, 96 or 99 wherein said
25 step of flowing an amount of liquid from said reservoir to said metering chamber through said inlet unidirectional valve comprises the step of flowing said amount of liquid through at least one liquid flow opening and a membrane of said inlet unidirectional valve.
- 30 165. A method of dispensing liquid according to claim 164 and further comprising the step of creating a seal when said inlet valve is closed.

166. A method of dispensing liquid according to claim 96 wherein said step of displacing said flexible diaphragm from a compressed position to an uncompressed position comprises the step of horizontally displacing said flexible diaphragm from a compressed position to an uncompressed position.

5

167. A method of dispensing liquid according to claim 99 wherein said step of displacing at least part of said compressible metering chamber from a compressed position to an uncompressed position comprises the step of horizontally displacing at least part of said compressible metering chamber from a compressed position to an uncompressed position.

10

168. A method of dispensing liquid according to claim 91 or 167 wherein said step of horizontally displacing at least part of said compressible metering chamber from a compressed position to an uncompressed position comprises the step of moving a substantially vertical diaphragm in a horizontal direction.

15

169. A method of dispensing liquid according to claim 90 or 166 wherein said step of horizontally displacing said flexible diaphragm from a compressed position to an uncompressed position comprises the step of moving a substantially vertical diaphragm in a horizontal direction.

20

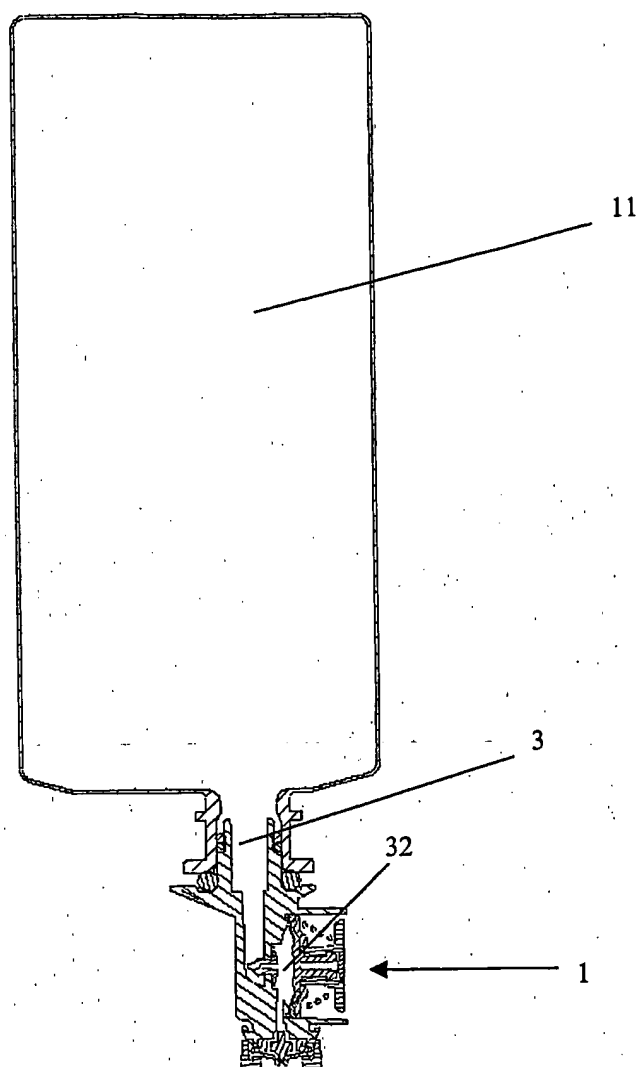


Fig. 1

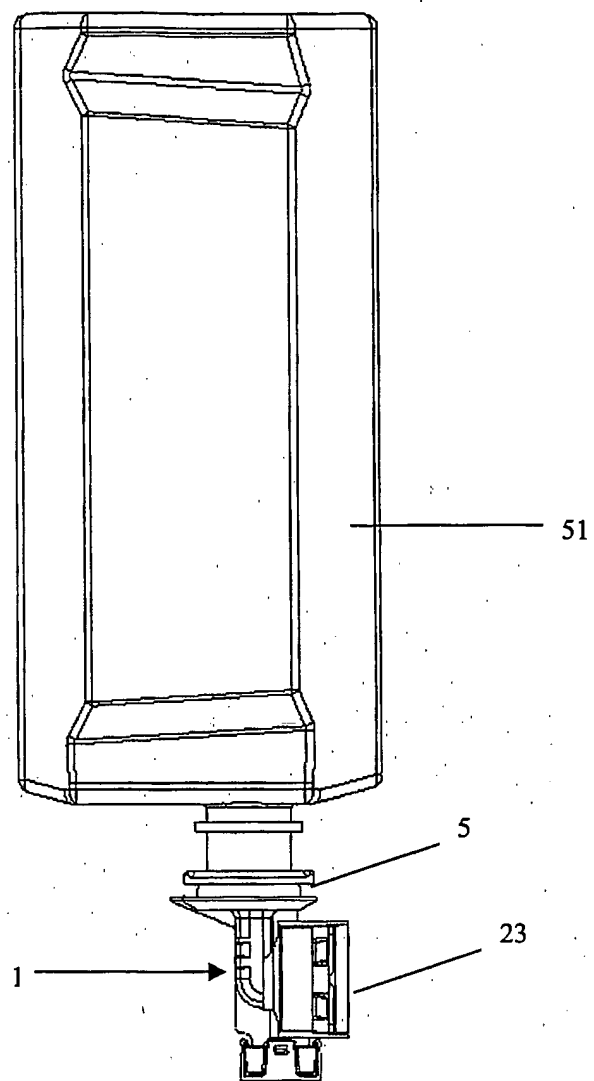


Fig. 2

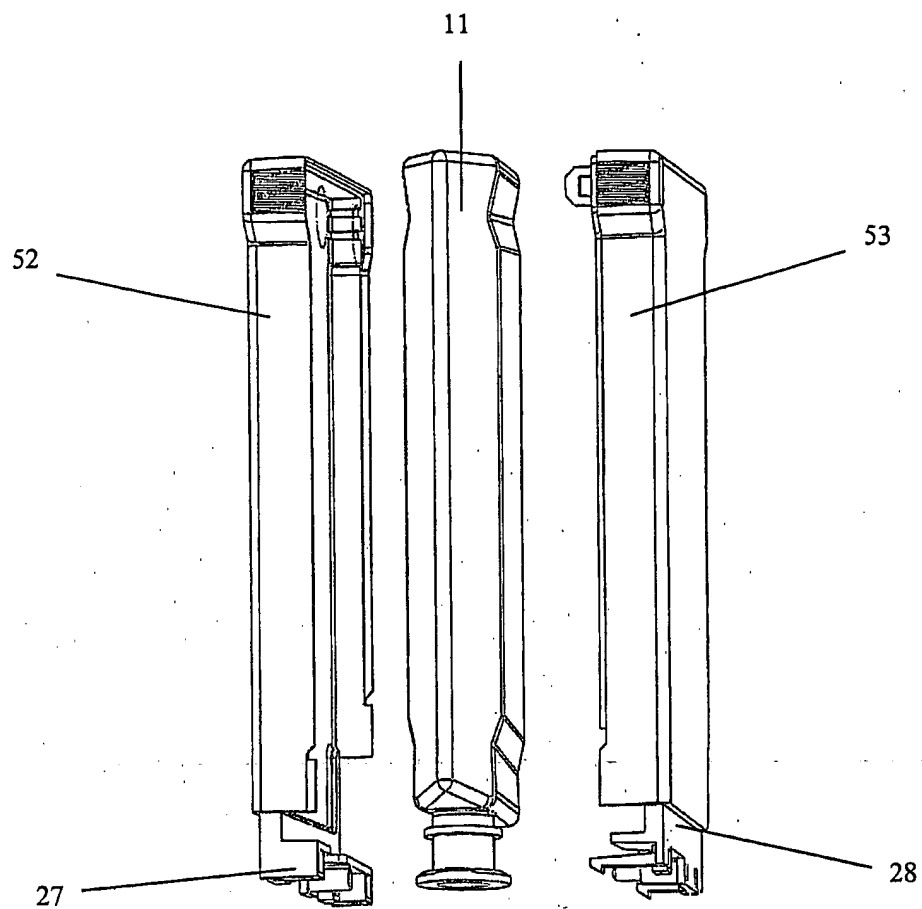
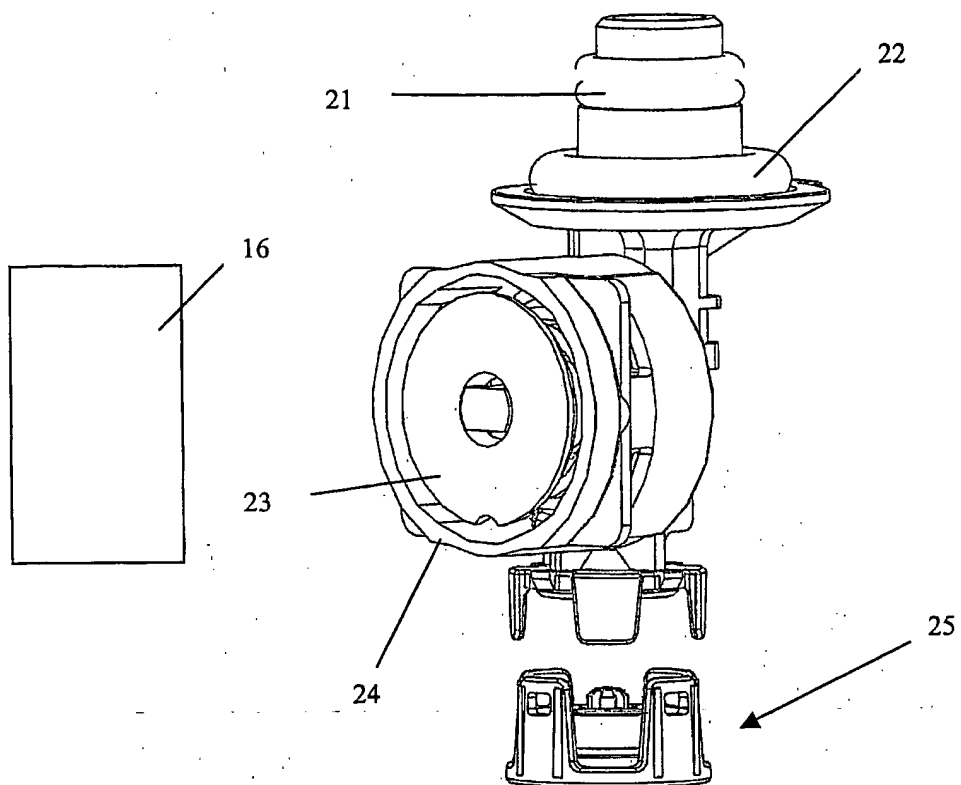


Fig. 3

**Fig. 4**

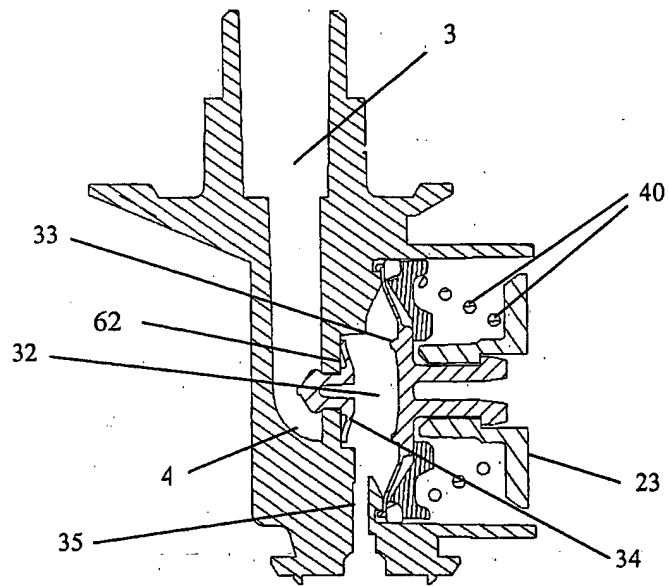


FIG. 5

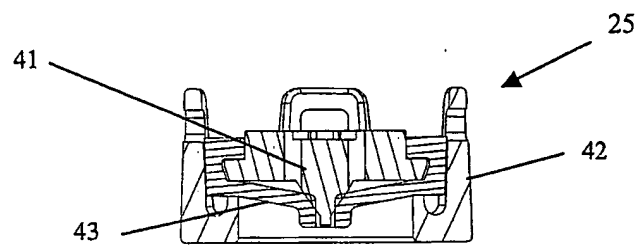


FIG. 6

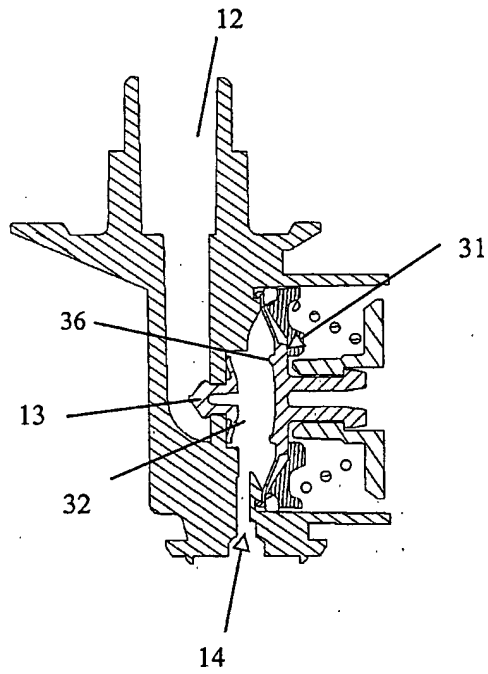


FIG. 7

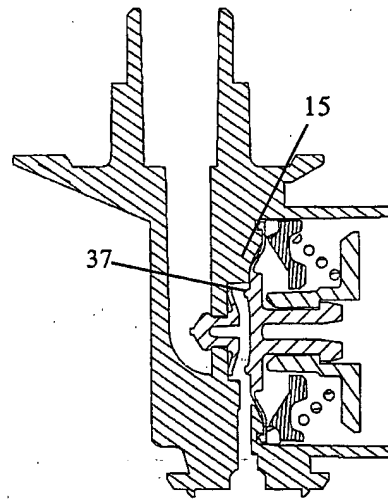


FIG. 8

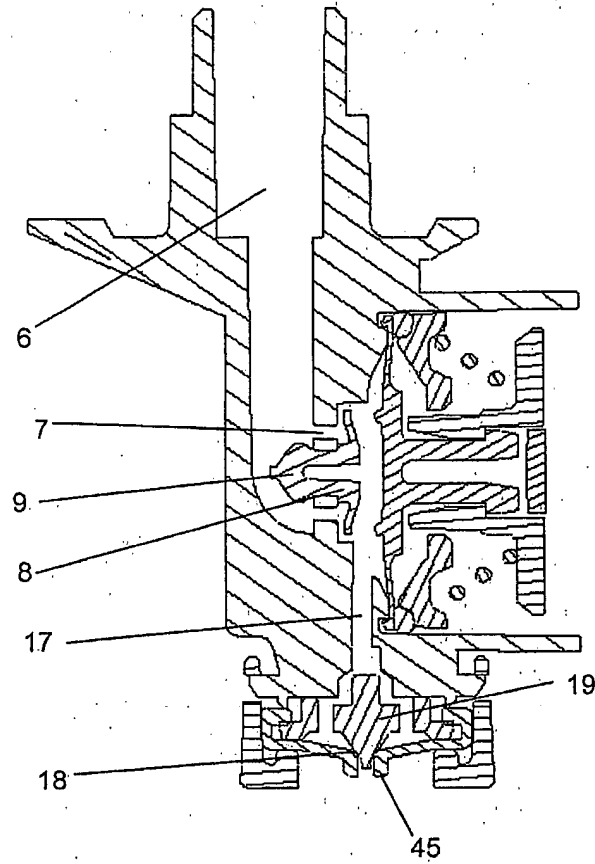


Fig. 9

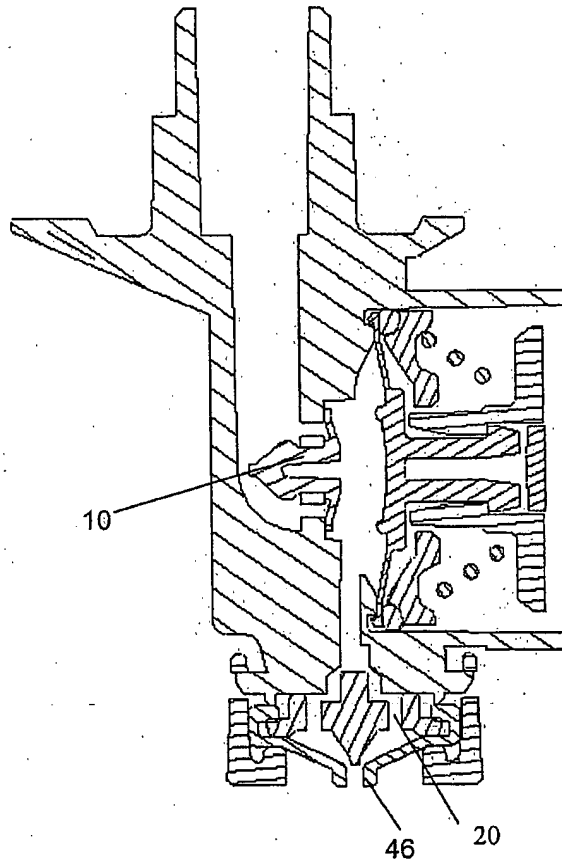
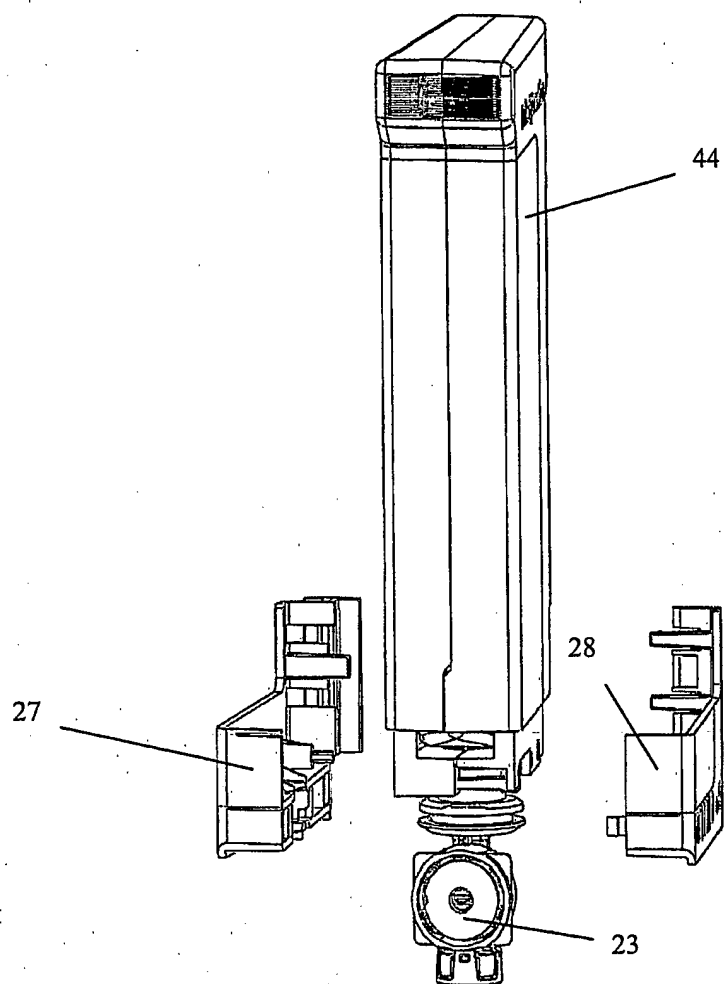


Fig. 10

**Fig. 11**

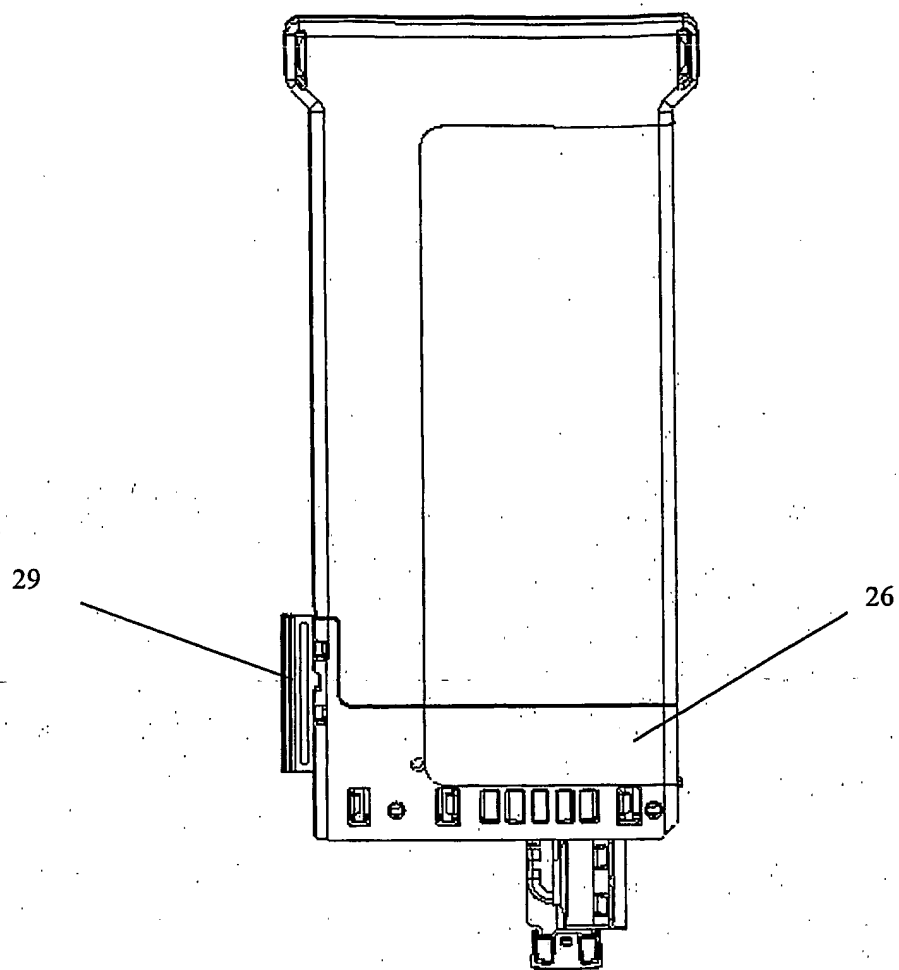


Fig. 12

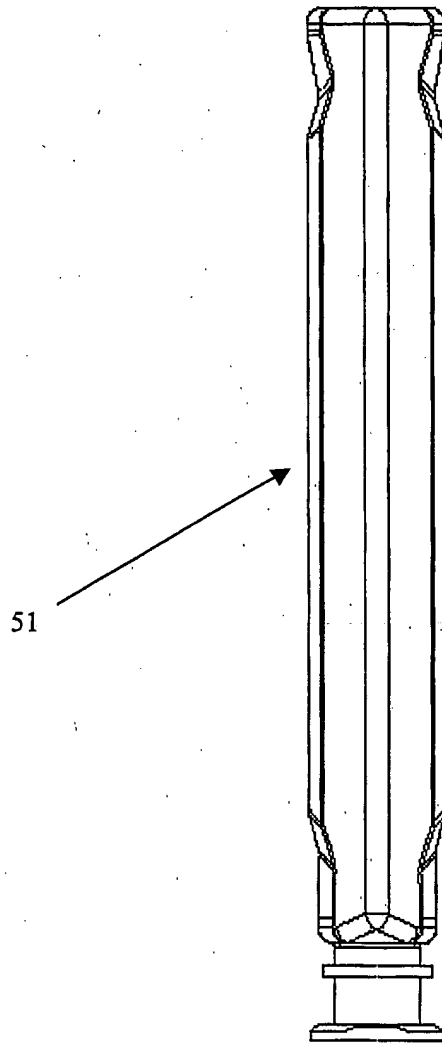


Fig. 13

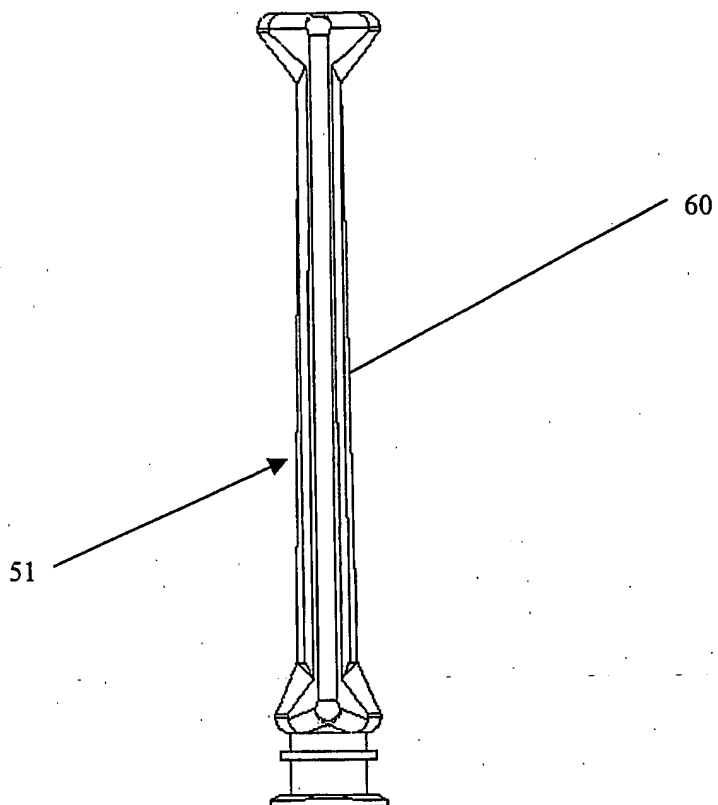


Fig. 14